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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/099,830	03/13/2002	Philip John Burke	ERD 100 CON	4061

23579 7590 07/26/2005

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EXAMINER

FETTEROLF, BRANDON J

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 07/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/099,830

Applicant(s)

BURKE ET AL.

Examiner

Brandon J. Fetterolf, PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 18 May 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 34 and 41-44 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 34 and 41-44 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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Burke et al.

***Response to Amendment***

The Amendment filed on 05/18/2005 to the Final Office Action of 01/18/2005 is acknowledged and has been entered.

***Application Status***

The Finality of the Office Action filed on 01/18/2005 has been withdrawn.

Currently, Claims 34 and 41-44 are pending and under consideration.

**The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.**

**All rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.**

**New Rejections:**

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 34 and 41-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Friedlos et al. (Biochemical Pharmacology 1992; 44: 25-31, IDS) in combination with Norris et al. (Can. J. Chem. 1977; 55: 1687-1695).

Friedlos et al. teach the identification of novel reduced pyridinium derivatives as synthetic co-factors in the reduction of CB 1954 by the enzyme DT Diaphorase (page 28, 1<sup>st</sup> column, last paragraph, and Table 1). Specifically, the reference teaches (page 28, 2<sup>nd</sup> column) that the actual structural requirements in a co-factor of DT diaphorase are fairly lax and, indeed, it would appear that there is little requirement for the adenine nucleotide portion of NAD(P)H at all. Thus, the

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simplest quaternary (and therefore reducible) derivative of nicotinamide, 1-methylnicotinaide, was as good of a co-factor as NAD(P)H.

Friedlos et al. does not specifically identify other reduced pyridinium derivatives that are equivalent to the co-factors NRH in the reduction of CB1954 by DT diaphorase.

Norris et al. teach the identification and synthesis of pyridinium and dihydropyridine compounds which do not contain the adenine nucleotide portion of NADH (page 1687, 2<sup>nd</sup> column, 1<sup>st</sup> paragraph and Table 3). Specifically, the reference teaches a dihydropyridine compound consisting of 1-carbamoylmethyl-3-carbamoyl-1,4,-dihydropyridine (page 1688, 1<sup>st</sup> column (2i) and Table 3, i).

(Note: Claims 34 and 42-44 as drawn to a compound of formula I or formula II, encompasses 1-carbamoylmethyl-3-carbamoyl-1,4,-dihydropyridine: With regards to Claim 34, R<sup>1</sup> is a substituted alkyl substituted by CONH<sub>2</sub>, R<sup>2</sup> and R<sup>3</sup> are independently H, and R<sup>4</sup> is H. With regards to claim 43, R is a substituted alkyl consisting of CONH<sub>2</sub>. With regards to claim 43, the alkyl group is a C1 alkyl. With regards to claim 44, R is -CH<sub>2</sub>CONH<sub>2</sub>.

Claim 41 is drawn to a compound of formula 1, wherein the compound is 1-(carboxamidomethyl)-dihydronicotinamide which is another name for 1-carbamoylmethyl-3-carbamoyl-1,4,-dihydropyridine.)

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute NRH (or NADH) employed by Friedlos et al. with an equivalent analogue of NRH (or NADH) such as 1-carbamoylmethyl-3-carbamoyl-1,4,-dihydropyridine. One would have been motivated to do so because as taught by Friedlos et al, the actual structural requirements in a co-factor of DT diaphorase are fairly lax and, it would appear that there is little requirement for the adenine nucleotide portion of NAD(P)H. Thus, one of ordinary skill in the art would have a reasonably expectation of success that the substitution of NRH (or NADH) with an equivalent analogue of NRH (or NADH) as taught by Norris et al., one would achieve a series of co-factors for the reduction of CB 1954 by the enzyme DT Diaphorase.

Therefore, NO claim is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD  
Examiner  
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BF



**GARY B. NICKOL, PH.D.**  
**PRIMARY EXAMINER**